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| 10/505,375 | 05/10/2005 | Yuman Fong | 08582/014002 | 5371 |

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

WHITEMAN, BRIAN A

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1635

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-------------------------------|-----------------------------|--|
| Office Action Summary | Application No. 10/505,375 | Applicant(s) FONG ET AL. | |
| | Examiner Brian Whiteman | Art Unit 1635 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) 14, 22, 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>8/20/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Non-Final Rejection

Claims 1-14 and 22-23 are pending.

The cancellation of claims 15-21 and 24-27 and the amendment to claim 1 in paper filed on 11/17/05 is acknowledged and considered by the examiner.

The examiner has considered the International Search Report.

Election/Restrictions

Applicant's election with traverse of Group I and the species immunomodulatory proteins and chemotherapy in the reply filed on 11/17/05 is acknowledged. The traversal is on the ground(s) that claim 1 has now been amended to specify a technical feature that is not disclosed or suggested in the document cited by the Office action. This is not found persuasive because the technical feature linking groups appears to be surgically resecting a tumor from a subject and administering an attenuated, replication-competent, oncolytic herpes virus to the site of the surgical resection and not preventing or treating metastasis of cancer in a subject. As stated in the election/restriction, US 20020071832 teaches administering a replication competent herpes virus into resected tumor bed to ensure destruction of any remaining tumor cells (pages 5-6). Therefore, the technical feature linking the inventions of groups I-II does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

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It is noted that applicants did not include a list of claims readable on the elected species. To help expedite prosecution of the instant application, a list of claims readable on the elected species should be included with the response to the instant office action.

Claims 14, 22, and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and cytotoxins, tumor antigens, antisense nucleic acid molecules and ribozymes in claim 11 and biological therapy, radiation therapy, and gene therapy in claim 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 11/17/05.

Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 6-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the

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relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation 'method of preventing or treating metastasis of cancer in a subject' in amended claim 1 and claims dependent therefrom is not supported by the instant specification. Applicant has not pointed out where the amended claims are supported, nor does there appear to be a written description of the claim limitation 'method of preventing or treating metastasis of cancer in a subject' in the application as filed. See MPEP § 2163.06. The examiner has thoroughly searched the specification and cannot find support for the limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 6, and 8-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Fong et al. (US 20020071832, cited on a PTO-1449).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

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inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Fong teaches a method of resecting a tumor from a patient and injecting a virus into the tumor bed to ensure destruction of any remaining tumor cells (page 5). Fong teaches the limitation in instant claim 6 (page 4). Fong teaches the limitation in claim 8 (page 5). Fong teaches the limitation in instant claim 10 and 11 (page 4). Fong teaches the limitation in claims 12 and 13 (page 6).

Claims 1, 2, 3, 6, 8, 9, and 12-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Molnar-Kimber et al. (US 6,428,968, cited on PTO-1449). Molnar-Kimber teaches killing tumor cells of a subject comprising administering a replication-competent herpes virus and a chemotherapeutic agent to the subject (columns 21-24). The method can be used following surgical excision or for inhibiting growth of immature metastases by killing tumor cells distributed throughout the body (column 2). Molnar-Kimber teaches the limitation in claim 6 (columns 2 and 21-24). Molnar-Kimber teaches the limitation in claim 8 (column 23).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, and 7 are rejected under 35 U.S.C. 103(a) as being obvious over Fong et al. (US 20020071832, cited on a PTO-1449) taken with Wong et al. (Human Gene Therapy, 253-265, 2001, cited on a PTO-1449).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter

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disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Fong teaches a method of resecting a tumor from a patient and injecting a virus into the tumor bed to ensure destruction of any remaining tumor cells (page 5). Destruction of any remaining tumor cells would read on the preamble of the claim because destruction of remaining tumor cells would prevent tumor cells from metastasizing from the tumor bed. Fong teaches the limitation in instant claim 6 (page 4). However, Fong does not specifically use the NV1023 as the herpes virus in the method.

However, at the time the invention was made, that NV1023 is an oncolytic HSV vector designed to express the murine GM-CSF and murine IL-12 genes and NV1023 demonstrated infection efficiency, viral replication and cytotoxicity comparable to other HSV (page 253).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fong taken with Wong, namely to use NV1023 in the method taught by Fong. One of ordinary skill in the art would have been motivated to use NV1023 as the oncolytic herpes virus in the method because NV1023 was readily available to one of ordinary skill in the art for use in treating cancer in a subject and

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would save time for one of ordinary skill in the art from constructing and testing another attenuated, replication-competent, oncolytic herpes virus.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1, 6, 7, and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Molnar-Kimber et al. (US 6,428,968, cited on a PTO-1449) taken with Wong et al. (Human Gene Therapy, 253-265, 2001, cited on a PTO-1449). Molnar-Kimber teaches killing tumor cells of a subject comprising administering a replication-competent herpes virus and a chemotherapeutic agent to the subject (columns 21-24). The method can be used following surgical excision or for inhibiting growth of immature metastases by killing tumor cells distributed throughout the body (column 2). Molnar-Kimber teaches the limitation in claim 6 (columns 2 and 21-24). Molnar-Kimber teaches the limitation in claim 8 (column 23). However, Molnar-Kimber does not specifically using the NV1023 as the herpes virus in the method.

However, at the time the invention was made, that NV1023 is an oncolytic HSV vector designed to express the murine GM-CSF and murine IL-12 genes and NV1023 demonstrated infection efficiency, viral replication and cytotoxicity comparable to other HSV (page 253). The vector is used to enhance treating tumor in a subject (page 253).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Molnar-Kimber taken with Wong, namely to use NV1023 in the method taught by Molnar-Kimber. One of ordinary skill in the art would

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have been motivated to use NV1023 as the oncolytic herpes virus in the method because NV1023 was readily available to one of ordinary skill in the art for use in treating cancer in a subject and would enhance the method. In addition, using NV1023 would save time for one of ordinary skill in the art from constructing and testing an attenuated, replication-competent, oncolytic herpes virus.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Molnar-Kimber taken with Wong, namely to use NV1023 expressing GM-CSF or IL-12 in the method taught by Molnar-Kimber. One of ordinary skill in the art would have been motivated to use NV1023 to enhance the method of treating cancer in a subject.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1 and 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al. (US 5,162,231) taken with Molnar-Kimber et al. (US 6,428,968) in further view of Johnston et al. (Ann. Thorac. Surg. 2001; 71:1120-5). Cole teaches:

Treatment of lung cancer has largely been unsuccessful and at times controversial. The practice of surgically resecting the tumor is the most successful of all treatments; however, in most cases the malignant lesions recur or metastasize. The use of radiotherapy and chemotherapy have also had limited success in prolonging the life of lung cancer patients. In fact, the median survival for a patient with small cell lung carcinoma, who is treated with chemotherapy and with or without radiation therapy is 10-

15 months in patients with "limited" disease, and 7-11 months in patients with "extensive" disease. See column 1.

However, Cole does not specifically teach administering an attenuated replication competent oncolytic herpes virus to the site of the surgical resection.

However, at the time the invention was made, Molnar-Kimber teaches killing tumor cells of a subject comprising administering a replication-competent herpes virus and a chemotherapeutic agent to the subject (columns 21-24). The method can be used following surgical excision or for inhibiting growth of immature metastases by killing tumor cells distributed throughout the body (column 2). Molnar-Kimber teaches that the method is for enhancing the treatment of lung cancer in a subject (column 3).

In addition, at the time the invention was made, Johnston teaches that a lung tumor spreads to lymph nodes (page 1120).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Cole taken with Molnar-Kimber in further view of Johnston, namely to administer an attenuated replication competent oncolytic herpes virus to the site of surgical resection in a lung. One of ordinary skill in the art would have been motivated to combine the teaching to enhance the treatment of lung cancer in a subject, wherein the lung cancer has been resected.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Cole taken with Molnar-Kimber in further view of Johnston, namely to treat cancer that has metastasized from the lung to the lymph node of the subject. One of ordinary skill in the art would have been motivated to

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combine the teaching to enhance the treatment of lung cancer that has metastasized to the lymph node because one of ordinary skill in the art understands that lung cancer spreads to the lymph nodes as exemplified by Johnston (page 1120) and Molnar-Kimber teaches using herpes virus and a chemotherapeutic agent for inhibiting growth of immature metastases by killing tumor cells distributed throughout the body.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

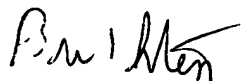
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Brian Whiteman
Patent Examiner, Group 1635

A handwritten signature in black ink, appearing to read "Brian Whiteman", written in a cursive style.